PRESCRIBING INFORMATION

OSTO-D_2 CAPSULE

DIETARY VITAMIN SUPPLEMENTS
&
VITAMINS FOR THERAPEUTIC USE

PRODUCT LIST:

TRITON PHARM PRODUCT	MARKET EQUIVALENT	ACTIVES (per mL or tablet)	EXCIPIENTS (Triton Pharma only)
Osto-D_2 Capsule	Ostoforte	Vitamin D_2 50,000 IU	Soybean Oil NF

VITAMINS – Sources, Functions, Dosage, Deficiency, Toxicity

All living things need vitamins for health, growth, and reproduction. They are not a source of calories and do not contribute significantly to body mass. They are used as tools in processes that regulate chemical activities in the organisms that use basic elements- carbohydrates, fats, and proteins- to form tissues and to produce energy. Vitamins can be reused and only tiny amounts are needed to replace those that are lost. Most vitamins are essential in diet since the body does not produce enough of them or, in many cases, does not produce them at all.

Proteins, carbohydrates, and fats combine with other substances to yield energy and build tissues. These chemical reactions are catalyzed, or accelerated, by enzymes produced from specific vitamins, and they take place in specific parts of the body. The water-soluble vitamins are absorbed by the intestine and are carried by the circulatory system to the specific tissues where they will be put into use. The B vitamins act as coenzymes, compounds that unite with a protein component called an apoenzyme to form an active enzyme. The enzyme then acts as a catalyst in the chemical reactions that transfer energy from the basic food elements to the body. It is not known if vitamin C acts as a coenzyme.

Because water-soluble vitamins are not stored in the body in appreciable amounts, a daily supply is essential to prevent depletion.

The intestine absorbs fat-soluble vitamins, and the lymph system carries them to the different parts of the body. Fat-soluble vitamins are involved in maintaining the structure of cell membranes and are responsible for the synthesis of certain enzymes. The body can store larger amounts of fat-soluble vitamins. The liver provides the chief storage tissue for vitamins A and d, while vitamin E is stored in body fat and to a lesser extent in reproductive organs. Relatively little vitamin K is stored. Excessive intake of fat-soluble vitamins, particularly A and D, can lead to toxic levels in the body.

Many vitamins work together to regulate several processes within the body. A lack of vitamins can upset the body's balance or block one or more metabolic reactions.

Vitamin B complex consists of several vitamins that are grouped together because of the loose similarities in their properties, distribution in natural sources, and physiological functions. Most of the B vitamins have been recognized as coenzymes, and they all appear to be essential in facilitating the metabolic processes of all forms of animal life.

In technologically advanced societies, vitamin deficiency results mainly from poverty, food faddism, , misuse of drugs, chronic alcoholism, or prolonged parenteral feeding. Vitamin dependency results from a genetic defect in the metabolism of the vitamin or in the binding of the vitamin-related coenzyme to its apoenzyme. In some instances, vitamin doses as high as 1000 times the recommended dietary allowance (RDA) improve the function of the altered metabolic pathway. Persons with vitamin dependency have been identified for vitamin D, thiamine, niacin, vitamin B_6, biotin, and vitamin B_{12}.

Megavitamin therapy is a cause of vitamin toxicity (hypervitaminosis) for vitamins A, D, E, C and B_6, for niacin, and for folic acid (folate).

Patients on long-term dialysis commonly receive multivitamin supplements (to replace estimated dialytic loss of the water-soluble vitamins B-complex, folic acid and vitamin C.

Vitamin like substances includes a number of compounds that resemble vitamins in their activity but are normally synthesized in the body in adequate amounts. They are often classified with the B vitamins because of similarities in function and distribution in foods. Their status as essential nutrients remains unclear. Choline is found in all living cells and plays a role in nerve function and various metabolic processes. Myoinositol is a water-soluble compound; its significance in human nutrition is not established. Para-aminobenzoic acid is an integral part of folic acid but its role in human nutrition has not been documented. Carnitine has an essential role in the transport of fatty substances. Lipoic acid seems to have a coenzyme function similar to that of thiamine; however, because it is synthesized in the liver and kidneys, it is not considered a vitamin. Bioflavinoids are a group of substances that affect the permeability of capillaries but do not normally have to be added to diets.

NUTRIENT	SOURCES	FUNCTIONS	USUAL DOSAGE
Vitamin D (Cholecalciferol, ergocalciferol) **Fat soluble**	It is both a hormone and a vitamin. Occurs mainly in 2 forms: ergocalciferol (activated ergosterol vitamin D_2), found in irradiated yeast; and cholecalciferol (activated 7-dehydrocholesterol, vitamin D_3), formed in human skin by Ultraviolet irradiation of the skin (main source), and found in fish liver oils and egg yolks, fortified milk (main dietary source), butter, egg yolk, and liver. Synthesis in the skin is normally the major source. Vitamin D_3 is not itself biologically active, but must be modified by the body to have any physiological effects. Fat in the intestine is necessary for vitamin D absorption through the intestinal wall and then storage in the fat cells in the liver, skin, brain, and bones in sufficient amounts.	Vitamin D is a prohormone with several active metabolites that act as hormones. In the skin previtamin D_3 is synthesized and then isomerized to vitamin D_3 and then converted to $25(OH)D_3$ (calcitriol) the major circulating form. It passes through the enterohepatic circulation and is reabsorbed from the gut. Principally in the kidneys, it is further hydroxylated to the much more metabolically active form $1,25(OH)_2D_3$. The main function of the vitamin D hormone is to increase the Calcium absorption from the intestine, resorption, mineralization, maturation of bone, and tubular reabsorption of calcium. In the intestine it enhances Ca and PO_4 transport (absorption) In the kidneys it enhances Ca reabsorption by the tubule; it inhibits the synthesis of 1α-hydroxylase; it stimulates the synthesis of 24-hydroxylase. In the bone it stimulates osteoblasts to produce more alkaline phosphatase and osteocalcin (a vitamin K-dependent bone protein) and less collagen, all of which favour bone formation; it stimulates (at higher doses) mononuclear cells to differentiate into macrophages, which fuse with osteoclasts and increase Ca mobilization. In the parathyroid glands it inhibits PTH secretion In the lymphomedullary system it stimulates immunogenic and antitumor activity. Plays a role in the secretion of insulin in the pancreas, thus in the regulation of blood sugar. Regulates calcium levels in the blood for normal nerve impulse	**-Primary deficiency** 2,000 to 8,000 IU / day vitamin D_3 for 3 weeks. **-Metabolic deficiency** 1-2 mcg / day of $1,25(OH)_2D_3$ or 1α-OH-D_3 400 IU / day may be required for lactating mothers whose diet is inadequate, especially in the winter. Vitamin D deficiency rickets responds to as little as 400 IU/day of vitamin D_2 or D_3. If frank osteomalacia is present, 5000 IU/day vitamin D_2 or D_3 is given for 6-12 weeks and then reduced to 400 IU/day. Additional treatment with 2g Ca / day is desirable during the early stages of treatment. Type I vitamin D dependent rickets responds to physiologic doses of calcitrol 0.25-1.0mcg / day po. Type II vitamin D dependent rickets treatment depends on the severity of bone lesions and hypocalcemia. Up to 6mcg / Kg body weight or a total of 30-60mcg / day of calcitriol in addition to up to 3g of Ca daily is needed in the most severe cases. Treatment with vitamin D requires monitoring of plasma Ca levels; although hypercalcemia may result, it generally responds quickly to adjustment in the dose of vitamin D.

		transmission and muscle contraction. Used to treat renal osteodystrophy caused by chronic renal failure. Calcitriol has been found to induce differentiation and/or inhibit proliferation of a number of cancerous and non-cancerous cell types. Anticonvulsanta increase the metabolism of calcitriol in the liver, thereby increasing the requirement for vitamin D of individuals on long-term anticonvulsant therapy. Cholestyramine, a bile acid binding resin used to treat elevated cholesterol levels, and mineral oil can decrease the intestinal absorption of vitamin D. The induction of hypercalcemia (elevated blood calcium levels) by toxic levels of vitamin D may precipitate cardiac arrhythmia in patients on digitalis or verapamil, a calcium channel blocker, used to treat high blood pressure. It is involved in normal cell growth and maturation.	

NUTRIENT	DEFICIENCY	TOXICITY
Vitamin D	Rickets, a weakening and softening of the bones and muscle due to extreme Ca loss, (sometimes with tetany), osteomalacia. Metabolic bone disease resulting from vitamin D deficiency is called **Rickets** in children and **Osteomalacia** in adults. These diseases result from common pathogenetic factors but differ in their clinical and pathologic expression because of the differences between growing and mature bones. Inadequate exposure to sunlight and low dietary intake are usually necessary for development of clinical vitamin D deficiency. Deficiency may also be caused by defects in the production of $25(OH)D_3$ or the action of $1,25(OH)_2D_3$. Deficiency may occur in hypoparathyroidism, in hereditary diseases such as familial hypophosphatemic rickets, an X-linked dominant disorder and in various other diseases. Maternal osteomalacia can lead to metaphyseal lesions and tetany in the newborn. Infants are restless and sleep poorly. They have reduced mineralization of the skull, away from the sutures. Sitting and crawling are delayed as is fontanelle closure, and there is bossing of the skull and costochondral beading (rachitic rosary). In children aged 1-4 years, epiphyseal cartilages at the lower ends of the radius, ulna, tibia, and fibula enlarge; kyphoscoliosis develops, and walking is delayed. In older	Toxicity, called hypervitaminosis D results primarily from vitamin D supplementation over many years at pharmacological doses of 10,000-50,000 IU/day. The adverse effects of hypervitaminosis D appear to be due mainly to the elevated blood calcium levels it induces. Vitamin D 40,000 IU/day produces toxicity within 1-4 months in infants and as little as 3000 IU/day can produce toxicity over years. Toxic effects have occurred in adults receiving 100,000 IU/day for several months. Elevated serum Ca levels of 12-16mg/dL (3-4 mmol/L) are a constant finding when toxic symptoms occur The first symptoms are anorexia, nausea, and vomiting, followed by polyuria, polydipsia, weakness, nervousness, and pruritus. Renal function is impaired. Metastatic calcifications may occur, particularly in the kidneys. Plasma $25(OH)D_3$ levels are elevated as much as 15 fold in vitamin D toxicity, whereas $1,25(OH)_2D_3$ levels are usually within the normal range. Treatment consists of discontinuing the vitamin, providing a low-calcium diet, keeping the urine acidic, and giving corticosteroids. Kidney damage or metastatic calcification, if present, may be irreversible. Exogenous vitamin D in pharmacological doses produces excessive bone resorption as well as increased intestinal Ca absorption and hypercalciuria. In sarcoidosis, the hypercalcemia and hypercalciuria

	children and adolescents, walking is painful, and in extreme cases, such deformities as bowlegs and knock-knees develop. Rachitic tetany is caused by hypocalcemia and may accompany infantile or adult vitamin D deficiency. In adults, demineralization (osteomalacia) occurs, particularly in the spine, pelvis, and lower extremities. Regulates bone mineral density and a deficiency may lead to osteoporosis, a disease in which bones become lighter, less dense and more prone to fractures. Bone loss is also associated with rheumatoid arthritis. Low levels of vitamin D have been linked to several cancers including those of the colon, prostrate, and breast Abnormalities in vitamin D may be linked to multiple sclerosis. Deficiency impairs glucose metabolism by reducing insulin secretion. This is likely to increase the risk of diabetes mellitus.	appear to be due to unregulated conversion of $25(OH)D_3$ to $1,25(OH)_2D_3$. Idiopathic hypercalcemia of infancy is due to a group of rare genetic disorders, all of which are associated with increased intestinal absorption of Ca and may result from vitamin D toxicity or increased sensitivity to vitamin D. Nephrotoxicity is indirectly caused by vitamin D, milk, alkali, and vitamin D analog through the mechanism of nephrocalcinosis and lithiasis.

LABORATORY TESTS USED TO EVALUATE NUTRITIONAL STATUS

- Complete blood count, including hematocrit, hemoglobin, RBC, red cell indexes, WBC, lymphocytes, and differential count
- Plasma proteins, including albumin, globulin, prealbumin, transferring, and retinal binding protein.
- Plasma nitrogen, BUN, creatinine, uric acid.
- Plasma lipids, including total cholesterol, triglycerides, LDL cholesterol, and HDL cholesterol.
- Plasma electrolytes: Na^+ , K^+ , Cl^- , HCO_3^{2-} , Mg^{2+} , Ca^{2+} , HPO_4^{2-}
- Vitamins and vitamin-dependent substances: vitamin A, vitamin E, $25(OH)D_3$, vitamin K, vitamin C , folate , and vitamin B_{12} in plasma; thiamine, riboflavin, and N'-methylnicotinamide in urine; and transketolase and glutathione reductase in RBCs.
- Minerals; iron, zinc, copper, and manganese in plasma; sodium, zinc, copper, manganese, and phosphorous in urine.
- Urinary nitrogen, urea, creatinine, uric acid, hydroxyproline, 3-methylhistidine
- Skin tests for antigens (to assess cell-mediated immunity)

Imaging procedures and biochemical laboratory tests are useful in appraising nutritional status. X-rays of the thorax and the skeleton are used to determine cardiopulmonary function and bone density. GI disturbances secondary to malnutrition can be suited radiographically with contrast media. CT and MRI are useful in viewing soft tissue.

Modern analytical instrumentation with high-pressure liquid chromatography, radioimmuno assay of enzymes, or flame photometry has greatly improved the sensitivity and specificity of biochemical tests of nutritional status. Measuring plasma levels or urinary excretion of proteins, lipids, electrolytes, trace minerals, and vitamins can provide evidence about body stores of these nutrients. Nutrient-dependent enzymatic tests can be applied to both red and white blood cells, and the immune status can be appraised by determining lymphocyte counts, immunoglobulin levels, and the response of lymphocytes to mitogens and by performing skin tests (see above).

PRODUCTS- Indications

PRODUCT	INDICATIONS
Osto-D_2 Capsule	Treatment of refractory rickets (Vitamin D resistant Rickets), familial phosphatemia and hypoparathyroidism

MALNUTRITION

Malnutrition results from imbalance between the body's needs and the intake of nutrients, which can lead to syndromes of deficiency, dependency, toxicity, or obesity. Malnutrition includes under nutrition, in which nutrients are undersupplied, and over nutrition, in which nutrients are oversupplied. Under nutrition can result from inadequate intake; malabsorption; abnormal systemic loss of nutrients due to diarrhea, hemorrhage, renal failure, or excessive sweating; infection; or drug addiction. Over nutrition can result from overeating; insufficient exercise; over prescription of therapeutic diets, including parenteral nutrition; excess intake of vitamins, particularly pyridoxine (vitamin B_6), niacin, and vitamins A and D; and excess intake of trace minerals.

Because of the high demand for energy and essential nutrients, infants and children are at particular risk of under nutrition. Protein-energy malnutrition in children consuming inadequate amounts of protein, calories, and other nutrients is a particularly severe form of under nutrition that retards growth and development. Hemorrhagic disease of the newborn, a life-threatening disorder, is due to inadequate vitamin K. Deficiencies of iron, folic acid, vitamin C, copper, zinc, and vitamin A may occur in inadequately fed infants and children. In adolescence, nutritional requirements increase because the growth rate increases. Anorexia nervosa, a form of starvation, may affect adolescent girls.

Requirements for all nutrients are increased during pregnancy and lactation. Aberrations of diet, including pica (the consumption of nonnutritive substances, such as clay and charcoal), are common in pregnancy. Anemia due to folic acid deficiency is common in pregnant women, especially those who have taken oral contraceptives. Folic acid supplements are recommended for pregnant women to prevent neural tube defects (spina bifida) in their children. An exclusively breastfed infant can develop vitamin B_{12} deficiency if the mother is a vagan. An alcoholic mother may have a handicapped and stunted child with fetal alcohol syndrome, which is due to the effects of ethanol and malnutrition on fetal development.

A diminished sense of taste and smell, loneliness, physical and mental handicaps, immobility, and chronic illness can militate against adequate dietary intake in the elderly. Absorption is reduced, possibly contributing to iron deficiency, osteoporosis, and osteomalacia due to lack of vitamin D and absence of exposure to sunshine.

In patients with chronic disease, malabsorption states tend to impair the absorption of fat-soluble vitamins, vitamin B_{12}, calcium, and iron. Liver disease impairs the storage of vitamins A and B_{12} and interferes with the metabolism of protein and energy sources. Patients with kidney disease, including those on dialysis, are prone to develop deficiencies of protein, iron, and vitamin D.

	RISK FACTORS
UNDER NUTRITION	▪ Gross underweight- weight for height or BMI < 80% of standard ▪ Loss of 10% or more of body weight during a 3-month period. ▪ Alcohol intake of >6-oz equivalents of ethanol per day. ▪ No oral intake for > 10 days ▪ Protracted nutrient losses due to malabsorption syndromes, short-bowel syndromes, fistulas, diabetes, renal dialysis, draining abscesses, or wounds. ▪ Increased metabolic needs due to extensive burns, infection, trauma, protracted fever, or hyperthyroidism. ▪ Intake of drugs with antinutrient or catabolic properties, e.g., depressants, corticosteroids, immunosuppressants, antitumor drugs.
OVER NUTRITION	▪ Good appetite combined with lack of exercise and weight gain ▪ High-fat, high-salt diet ▪ Large doses of nicotinic acid for hypercholesterolemia ▪ Large doses of pyridoxine for premenstrual syndrome ▪ Large doses of vitamin A for skin disorders. ▪ Large doses of iron and other trace minerals without a medical prescription.

The diagnosis of malnutrition is based on results of the medical and diet history, physical examination, and selected laboratory tests. Results are compared with norms of weight for height, body mass index (BMI), dietary intake, physical findings, and plasma levels of nutrients and nutrient-dependent substances, such as hemoglobin, thyroid hormones, transferring, and albumin.

Starvation is the most severe form of malnutrition. It may result from fasting, famine, anorexia nervosa, and catastrophic disease of the GI tract, stroke, or coma. The basic metabolic response to starvation is conservation of energy and body

tissues. However, the body will mobilize its own tissues as a source of energy, which results in the destruction of visceral organs and muscle and in extreme shrinkage of adipose tissue. Total starvation is fatal in 8-12 weeks.

The amino acid carnitine is a methylated and further modified derivative of lysine. It is required for the transport of long chain fatty acyl coenzyme A esters into mitochondria. The human requirement is met by a combination of endogenous biosynthesis and dietary intake. Carnitine deficiency can cause muscle necrosis, myoglobinuria, lipid-storage myopathy, hypoglycemia, fatty liver, and hyperammonemia with muscle ache, fatigue, and confusion. Deficiency can result from a reduced capacity for its biosynthesis; subnormal levels of carnitine palmitoyltransferase; alteration in cellular mechanisms for carnitine transport; excess loss of carnitine due to diarrhea, diuresis, or hemodialysis; increased requirements of carnitine in states of ketosis and high demand for fat oxidation; and inadequate intake during long term TPN

Essential fatty acids (EFAs) requirements are 1-2% of dietary calories for adults and 3% for infants, with a suggested ratio of 10:1 for ω-6:ω-3 fatty acids. EFAs are needed for many physiologic processes, including maintaining the integrity of the skin and the structure of cell membranes and synthesizing prostaglandins and leukotrienes. Full-term babies fed a skim milk formula low in linoleic acid may have growth failure, thrombocytopenia, alopecia, and a generalized scaly dermatitis, which resembles congenital ichthyosis, with increased water loss from the skin. This syndrome is reversed by linoleic acid supplementation. Deficiency is unlikely to occur on balanced diets.

NUTRIENT-DRUG INTERACTIONS

Important nutrient-drug interactions include diet effects on drug disposition. Altered drug pharmacokinetics in nutritional deficiencies, drug-induced changes in appetite, and drug-induced malnutrition.

Individual food components can enhance, retard, or decrease drug absorption. For example, tyramine, a component of cheese and a potent vasoconstrictor, may lead to hypertensive crisis in some patients who take monoamine oxidase inhibitors and eat cheese. High-protein diets can enhance the rate of drug metabolism in part by stimulating the induction of cytochrome. Diets that alter the bacterial flora may markedly affect the overall metabolism of certain drugs.

Deficiency of such nutrients as calcium, magnesium, or zinc may impair drug metabolism. Energy and protein deficiencies reduce tissue levels of enzymes and may impair the response to drugs by reducing absorption and causing liver dysfunction. Drug response may also be affected by impaired absorption due to changes in the GI tract. Vitamin C deficiency is associated with decreased activity of drug-metabolizing enzymes. The frequency of adverse drug reactions in the elderly may be related to low vitamin C status.

Certain drugs affect vitamin metabolism. Ethanol impairs thiamine absorption, and isoniazid is a niacin and pyridoxine antagonist. Ethanol and oral contraceptives inhibit folic acid absorption. Most patients receiving phenytoin, Phenobarbital, primidone, or phenothiazines for long-term anti-convulsant therapy develop low serum and erythrocyte folate levels and occasionally megaloblastic anemia, probably because hepatic microsomal drug-metabolizing enzymes are affected. Folic acid supplements may interfere with the action of anticonvulsant drugs, but yeast tablets supplements seem to raise folate levels without this effect. Anticonvulsant-induced vitamin D deficiency is well recognized. Vitamin B12 malabsorption has been reported with amino salicylic acid, slow-release potassium iodide, colchicines, trifluoperazine, ethanol and oral contraceptives. Depression may occur in women taking oral contraceptives, usually with a high progestogen content. The mechanism is thought to be induction of tryptophan pyrolase, which results in the diversion of pyridoxine for niacin synthesis at the expense of 5-hydroxytryptamin neurotransmitter formation. Such patients usually respond to pyridoxine 25mg tid.

PRODUCT CONTRA-INDICATIONS

PRODUCT	CONTRA-INDICATIONS
0sto-D_2 Capsule	Hypocalcaemia, malabsorption syndrome, abnormal sensitivity to the toxic effects of Vitamin D, hypervitaminosis D, decreased renal function

INDIVIDUAL VITAMIN DOSAGES:

INGREDIENT	UNIT	Min/Day Under 6 Years A	Min/Day Over 6 Years B	Max/Day Non-therapeutic Level C	Max/Day All ages D
Vitamin D	IU	200.0	200.0	400.0	1000

PRODUCT DOSAGE:

PRODUCT	DOSAGE
Osto-D_2 Capsule	- For therapeutic use. -Recommended daily 400IU - Correction of deficiency 5,000 IU daily until biochemical and radiographic response is apparent - Vitamin D resistant Rickets 12,000-500,000 IU daily - Hypoparathyroidism 50,000 – 200,000 IU daily plus 4gm Calcium Lactate administered 6 times per day. - Dosage individualized under close medical supervision - Calcium intake should be adequate - Blood calcium, phosphorous and urea determinations must be made every 2 weeks, or more frequently if necessary

PRECAUTIONS- Products:

PRODUCT	PRECAUTIONS
Osto-D_2 Capsule	Keep out of reach of children. This product contains sufficient drug to seriously harm a child. Hypersensitivity to Vitamin D may be one etiological factor in infants with idiopathic hypercalcemia. In these cases Vitamin D must be seriously restricted. *Pregnancy:* Safety in excess of 400 IU of vitamin D daily during pregnancy has not been established and animal reproduction studies have shown fetal abnormalities associated with hypervitaminosis D. Avoid the use of vitamin D in excess of the recommended dietary allowance during pregnancy unless the potential benefits outweigh the possible adverse effects. Vitamin D ingestion from fortified foods, milk with vitamin D added, dietary supplements and other sources should be considered Readjust therapeutic dosage as soon as there is clinical improvement. Individualize dosage levels and exercise great care to prevent serious toxic effects. In vitamin D resistant Rickets, the range between the therapeutic and toxic doses is narrow. When high therapeutic doses are used, follow progress with frequent serum and urinary calcium (Sulkowitch test), potassium and urea determinations. In the treatment of hypoparathyroidism, calcium, parathyroid hormone and/or dihydrotachysterol may be required. Mineral oil interferes with the absorption of fat-soluble vitamins.

OVERDOSE – Products:

PRODUCT	SYMPTOMS	TREATMENT
Osto-D_2	Hypervitaminosis D is characterized by: - Hypercalcemia with anorexia, nausea, weakness, weight loss, vague aches and stiffness, constipation, diarrhea, convulsions, mental retardation, anemia, mild acidosis - Impairment of renal function with polyuria, nocturia, polydipsia, hypercalcuria, reversible azotemia, hypertension, nephrocalcinosis, generalized vascular calcification, irreversible renal insufficiency, albuminuria, or urinary casts. - Widespread calcification of the soft tissues, including the heart, blood vessels, renal tubules, and lungs. Bone demineralization (osteoporosis) in adults occurs concomitantly. - Decline in the average rate of linear growth and increased mineralization of bones in infants and children (dwarfism)	Immediate withdrawal of the vitamin, reduction of calcium intake and increased fluid intake. Hypercalcemic crisis requires vigorous treatment. Intravenous saline may quickly and significantly increase urinary calcium excretion. Other reported therapeutic measures include dialysis or the administration of citrates, sulfates, phosphates, corticosteroids, or EDTA.